In Vivo Bone Lead Measurement in Suburban Teenagers

Jane A. Hoppin, ScD*; Antonio Aro, PhD*‡; Howard Hu, MD, ScD*‡; P. Barry Ryan, PhD*§

ABSTRACT. *Objective.* **Bone represents a biologically active long-term storage site for lead, and bone lead data on teenagers are limited. Therefore, this study was designed to identify the distribution of bone lead in a teenage population and to explore the environmental and demographic factors associated with bone lead concentrations in young, nonoccupationally exposed subjects.**

Design. **A cross-sectional study of bone lead levels in high school students.**

Participants. **A total of 168 students at a suburban Boston high school. Subjects (90 boys, 78 girls) ranged in age from 13.5 to 19 years and included 40% nonwhite minorities. Of the 168 subjects, 45 lived in homes constructed before 1960. None of the participants reported a history of lead poisoning.**

Outcome Measures. **Tibial bone lead concentrations were measured in vivo for 60 minutes using K x-ray fluorescence. Lead exposure information was obtained by self-administered questionnaire.**

Results. **Point estimates of bone lead levels ranged from −7.15 to 14.23 μg lead/g bone mineral (μg/g), (mean, 4.0 μg/g; standard deviation, 4.4 μg/g). The reported measurement uncertainties accompanying each of the point estimates ranged from 2.56 to 9.01 μg/g (mean, 3.9 μg/g; standard deviation, 1.0 μg/g). Bone lead levels were not associated with the demographic factors of age, sex, or race. Additionally, current home conditions (housing age, traffic level) were not predictive of bone lead levels, even though these factors were predictive of in-home lead concentrations.**

Conclusions. **These results demonstrate that although bone lead levels are measurable in this age group, the common predictors of blood and bone lead concentrations are not explanatory for bone lead levels.** *Pediatrics* **1997;100:365–370;** ***lead, bone, environmental health, adolescents, environmental exposure, epidemiology.***

ABBREVIATIONS. XRF, x-ray fluorescence; SD, standard deviation.

Lead is a ubiquitous and persistent environmental contaminant. Although the introduction of lead into the environment has decreased dramatically, lead continues to be present in detectable quantities in both the environment and our bodies. Lead is found in most biological tissues including blood, teeth, bone, and hair.[1,2] These biological markers have been used to assess both recent and chronic lead exposure, because the half-life of lead varies among tissues. Recent exposure to lead can be detected by changes in blood lead concentration; the half-life of lead in blood is estimated to be ~35 days.[3] Chronic exposure to lead results in long-term storage of lead in bone; in adults, 95% of the body burden of lead is in bone.[4,5] The biological half-life of lead in the bones of adults ranges from 10 to 40 years.[6,7]

Until recently, measurement of bone lead concentrations was limited to cadavers and biopsy tissue. With the development of x-ray fluorescence (XRF) technology, the concentration of lead in bone now can be measured in living subjects. XRF has been used to measure lead in the bones of both occupationally exposed and environmentally exposed groups.[8–15] In studies of adults, bone lead levels have been significantly associated with age and integrated measures of blood lead levels over time.[8,10–12] In a large cross-sectional study of environmentally exposed subjects, 11 to 70 years of age, bone lead levels were significantly associated with age, decade of housing construction, and smoking.[10]

Teenagers represent a unique and understudied population for lead exposure assessment. Because most teenagers in the United States have grown up after the removal of lead from gasoline and paint and few have been occupationally exposed to lead, they represent a distinctive population in which to explore the impact of residual environmental lead levels on bone lead concentrations.

Two types of XRF instruments have been used for in vivo bone lead measurement in children: L-XRF and K-XRF.[15,11] L-XRF uses an x-ray generator and lower penetrating energies. By measuring lead primarily in subperiosteal surface bone, it has been postulated that L-XRF measurements reflect lead in a fairly mobilizable compartment of bone.[16] However, there are some concerns about the validity of this technique.[17] The K-XRF technique, which is used by our group and others,[8–11] derives an estimate of lead from the full thickness of bone, allowing for the estimation of the total body burden of lead. Because of concerns about the sensitivity of the K-XRF method, few investigations of bone lead levels have been conducted among teenage subjects.[1,10,11,18] In previous work, we demonstrated that by increasing the sensitivity of the bone lead scanner and doubling the sampling time, detectable bone lead levels could be measured among subjects 18 to 21 years of age.[11] Based on the ability to measure bone lead concentrations in young adults, we used this technology to

From the *Harvard School of Public Health, Boston, Massachusetts; ‡Channing Laboratories, Brigham and Women's Hospital, Boston, Massachusetts; and §Rollins School of Public Health, Emory University, Atlanta, Georgia.
Received for publication Nov 14, 1996; accepted Feb 11, 1997.
Reprint requests to (J.A.H.) Department of Environmental and Occupational Health, Rollins School of Public Health, Emory University, 1518 Clifton Rd NE, Atlanta, GA 30322.

measure bone lead concentrations in an even younger population: high school students.

MATERIALS AND METHODS

Subjects were recruited from classes at Randolph Junior/Senior High School in Randolph, MA, a suburban Boston community of 30 000 residents. Before volunteering for the study, students watched a short video about the project and received an information packet to review with their parents. Participation in the bone lead study involved completing a 12-page home characteristic survey, bone lead measurement, and completing another questionnaire on personal habits and diet during the 60-minute bone lead measurement. All study protocols and questionnaires were approved by the Harvard School of Public Health Human Subjects Committee.

Subjects were asked to complete the two questionnaires during the course of the study. The first, the Home History Survey, obtained information about current and former housing characteristics, basic demographics, and lead exposure history. This questionnaire was distributed in class and was designed to be completed by the teenage respondent with the assistance of her/his parents. The survey has been demonstrated to predict in-home dust and soil lead levels in this community.[19] The second questionnaire, the Activity Survey, was designed for this study to obtain information on personal habits that may contribute to lead exposure such as work experience and smoking. This questionnaire was filled out during the bone lead measurement.

The bone lead scanner operates on the principle of K-XRF and recently has been redesigned to improve the sensitivity of bone lead measurement, thereby allowing for bone lead measurement in nonoccupationally exposed younger individuals.[11,20] The technical specifications and validation data are described in detail elsewhere.[11,20] Briefly, the instrument uses a [^{109}]Cd γ-ray source of activity 1.11 GBq and a high-purity germanium detector in a back-scatter geometry.[20] γ and x-ray signals are shaped and digitized and then acquired by a multichannel analyzer board in a personal computer. At the completion of the measurement time, the data are automatically stored for analysis.

The effective radiation dose to the subject during an in vivo K-XRF measurement is very low and can be compared with natural background radiation.[21] The effective dose from a single K-XRF measurement of tibia is 0.2% and 0.1% of the average effective dose from a dental and chest x-ray, respectively. Similar dosimetry investigations of our apparatus have demonstrated even lower exposures, because the source strength is approximately half the strength of other bone lead scanners (2.2 vs 1.08 GBq). For our bone lead scanner, the estimated dose for a 60-minute measurement of a 15-year-old subject is 158 mrem.

Bone lead measurement occurred in a specially equipped room at the high school. During the appointment, the subject's height and weight were measured by the technician, the bone lead scanning procedure was explained in detail, and bone lead concentration was measured. For bone lead measurement, subjects were seated in a lead-free plastic resin chair, and the lower leg was restrained with Velcro straps to minimize movement during measurement. Bone lead measurements were taken from the midshaft of the left tibia for 60 minutes. The collimator was positioned perpendicular to and in the middle of the anterior tibial surface. If necessary, the bone lead scanner was paused to allow subject movement. During the sample collection time, subjects completed questionnaires, did homework, and listened to music. Technicians were present at all times during the measurement to answer questions.

In the [^{109}]Cd K-XRF technique, lead K x-rays are normalized to the elastic scatter peak; the elastic scatter peak is primarily attributable to elements of bone mineral rather than to elements of human soft tissue.[22] Normalization renders the accuracy of measurement relatively insensitive to variations in bone shape, size, and density; to overlying skin thickness; and to minor subject movement.[22] The precision of the measurement varies from person to person and depends primarily on the thickness of overlying tissue and the mass of bone mineral sampled.

The lead K x-ray peaks were extracted from the spectrum using the nonlinear least-square fitting technique based on the Marquadt[23] algorithm, with special fitting functions developed by the Birmingham University Group.[22] The fitting software generates the K x-ray counts to elastic scattering ratio for each of the K series x-rays. The final lead concentration was calculated using the means for the α_1 and β_1 peaks weighted by the inverse of their respective variances. The contributions of the different K x-rays to overall precision are discussed elsewhere.[22] Fig 1 presents the calibration curves used for in vivo bone lead measurement.

An estimate of measurement uncertainty accompanies each bone lead measurement made by K-XRF (for example, a tibia lead measurement may read 6.2 $\pm$ 3.5 μg/g bone mineral). The measurement uncertainty is derived by a goodness-of-fit calculation of the scatter in the XRF spectrum and represents an estimate of the standard deviation (SD) of multiple measurements. The fitting algorithm requires subtracting a fitted background curve from the actual data collected. Because of the statistical nature of the counting procedure, it is possible, especially for very low lead concentrations, that the value determined by subtracting the fitted background curve from the observed data is <0. This results in a negative value for the measured concentration. These values represent the best unbiased estimate of an individual's bone lead level.

Nine calibration standards ranging from 0.30 to 114 μg/g were prepared from plaster of paris, using known quantities of lead. These standards were used to create a calibration curve for the study. Five of the calibration standards used were of concentrations <25 μg/g, the anticipated concentration range for these subjects. The 5 μg/g standard was measured at least three times per week during the data collection period to evaluate drift in the calibration curve. No observable drift was identified during the 4 months of the study.

Statistical analyses, including descriptive statistics, two-sample tests, and analysis of variance, were performed to investigate the determinants of bone lead level in this teenage population. All statistical analyses were conducted using STATA 3.1.[24]

RESULTS

Approximately 500 students were approached in their classes about participating in the study. A total of 168 students (90 boys, 78 girls) had their bone lead measured during March 1995 through June 1995. Because of the hour-long measurement time and the 6-hour school day, this sample size represents the maximum number of participants possible during the study period. An additional 30 students completed questionnaires but could not be scheduled for bone lead measurement.

The study participants were demographically similar to the school as a whole. Subjects ranged in age from 13.4 to 18.9 years, with an average age of 16.4 years. The study population represents a diverse racial/ethnic mix. Approximately 27% of the population identified themselves as Black (African-American, Cape Verdean, Caribbean, or Haitian); 16% identified themselves as Asian; and 60% responded as being White. Because of multiple responses, percentages exceed 100. These values correspond well to the entire school's 1995 demographic statistics for grades 9 through 12 of 25% Black, 13% Asian, 55% White, and 7% Other race. There was no apparent difference in demographic characteristics between participants and other students at the school. Table 1 presents the demographic and environmental factors for the study population.

Questionnaires were used to obtain information on factors that may contribute to lead exposure such as housing age, traffic level, lead piping, and lead paint removal. Individuals were also asked about family history of lead poisoning. A large portion of the sample had lived in the community for the majority of their lives. A total of 31% of subjects sampled had lived in their house for their entire lives; an addi-

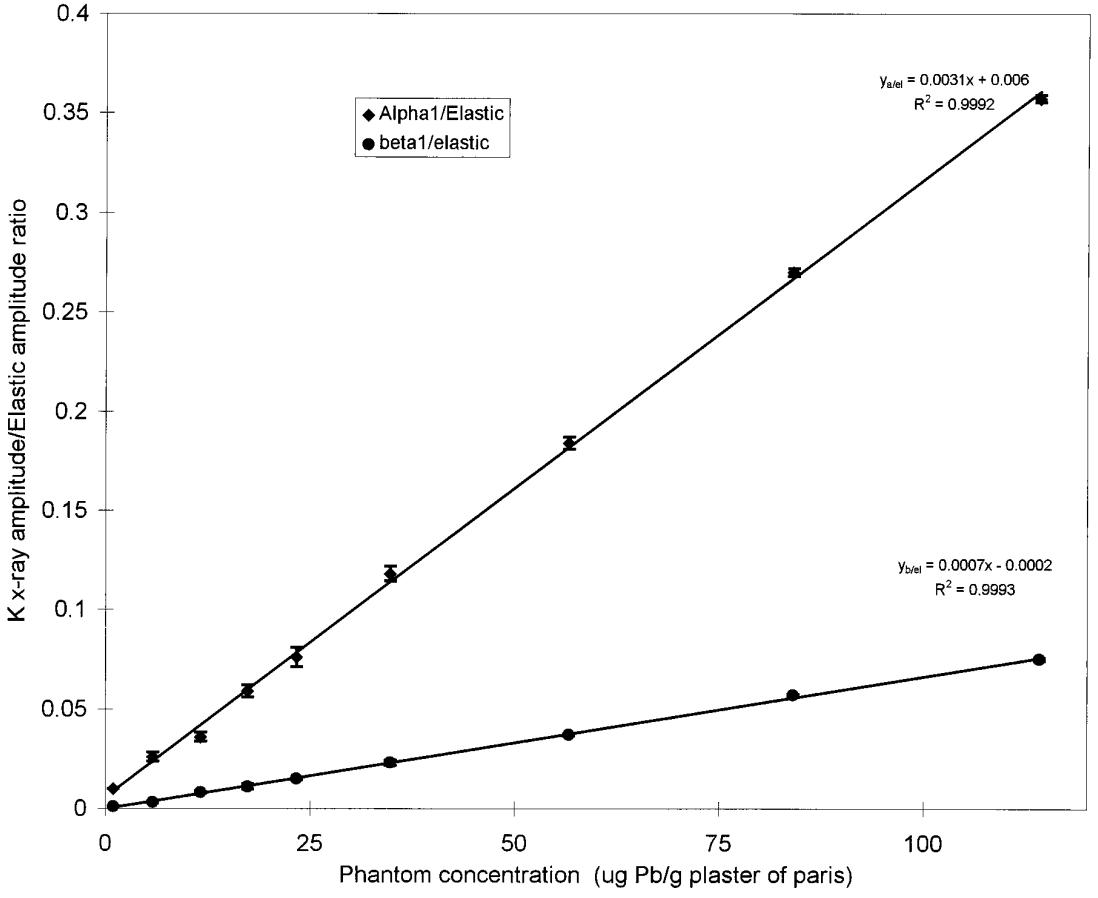

Fig 1. K-XRF calibration curves with error bars for the $K\alpha_1$ amplitude:elastic amplitude ratio and the $K\beta 1$ amplitude:elastic amplitude ratio used for in vivo bone lead measurement.

tional 36% had lived in their current residence >7 years. The housing stock in the community is diverse, ranging from pre-1900 to 1990s. A total of 27% reported living in homes constructed before 1960. Questions about lead piping and lead paint were noninformative. None of the subjects reported a history of lead poisoning, and only one subject reported that a family member had been lead poisoned.

The bone lead levels in this sample ranged from −7.15 to 14.23 μg lead/g bone mineral (μg/g), with a mean concentration of 4.0 μg/g and an SD of 4.4 μg/g. Bone lead levels were <1 μg/g for 24% of the sample; 8% of the population had bone lead levels >10 μg/g. Fig 2 presents the distribution of bone lead levels in this population. The reported measurement uncertainties accompanying each of the point estimates ranged from 2.56 to 9.01 μg/g (mean, 3.85 μg/g; SD, 1.02 μg/g).

Statistical analyses were performed to investigate the association between demographic variables and bone lead levels. No associations were observed for age, race, sex, income level, or home ownership in this population. Similar analyses were used to evaluate the influence of lead surrogate variables (housing age and traffic level) on bone lead levels; bone lead levels were not significantly different between levels of these predictors.

The reported measurement uncertainty was significantly associated with predictors identified previously for adults.[25] In *t* tests and correlation analyses, measurement uncertainty was significantly higher in girls (P = .0118), shorter subjects (P = .0002), and heavier subjects (P = .0103). Younger subjects had slightly higher measurement uncertainty (P = .09). Measurement uncertainty was independent of bone lead concentration. In multiple regression modeling of measurement uncertainty, white race, height, weight, and age explained 30% of the variance (P < .0001).

Measurement uncertainty represented a major portion of the population variance. The components of variance in the population were evaluated using the following measurement error model: $\sigma^2_t = \sigma^2_e + \sigma^2_b$, where σ^2_t = population variance (estimated by the observed variance), σ^2_e = error variance (estimated by the square of average measurement uncertainty), and σ^2_b = between-subject variance. This model assumed that the bone lead measurement and the measurement error were independent. The between-subject variance for this population was calculated to be (4.4 μg/g)^2 − (3.85 μg/g)^2 or (2.13 μg/g),^{2} indicating that measurement error is a major contributor to the variance in this population.

DISCUSSION

This study represents the largest sample of bone lead measurements for teenagers reported to date. The bone lead scanning technique was designed to consider the potentially low levels of bone lead and low bone mineralization of young subjects. How-

TABLE 1. Demographic and Environmental Characteristics of Study Population Participants at a Suburban Boston High School

Characteristic	Frequency	Percentage (%)
Sample size	168	100
Sex		
Boys	90	53.6
Girls	78	46.4
Race*		
African-American	22	13
Asian	27	16
Cape Verdean	6	3.6
Haitian	14	8.3
Hispanic	2	1.2
Native American	1	1.8
White	101	60
Other race	6	3.6
Annual income†		
<$15 000	3	2
$15 000–$29 999	10	6.5
$30 000–$49 999	34	22.2
$50 000–$75 000	48	31.4
>$75 000	24	15.7
Don't know	34	22.2
Home ownership		
Owner	144	87.3
Renter	21	12.7
Housing age		
pre-1940	15	9
1940–1949	8	4.9
1950–1959	22	13.3
1960–1969	24	14.6
1970–1979	38	23
post-1979	26	15.8
Don't know	32	19.4
Street traffic level		
Light traffic (residential)	128	76.2
Moderate traffic	30	17.8
Heavy traffic	10	6

* Total percentages for racial categories exceed 100% because subjects indicated >1 category.
† Only nonmissing responses included.

ever, unlike in the studies of adults[10,26–28] and in our previous study of young adults,[11] bone lead levels were not associated with age in this population. Additionally, bone lead concentration was not associated with any of the demographic variables collected, including sex and race. Without demographic factors influencing bone lead levels, it was anticipated that the influence of environmental surrogate variables, such as housing age and street traffic levels, would be easier to detect. However, bone lead levels were not associated with either housing age or street traffic levels, although both were predictive of in-home lead levels in 34 of the subjects' homes. Environmental sampling data and questionnaire validation are discussed in detail elsewhere.[19]

These data are consistent with bone lead levels reported in other teenage and young adult populations, both in vivo and in vitro, over the past 15 years. These studies are summarized in Table 2. Based on these results, there does not appear to be a discernible trend in bone lead levels in this age group over time. However, these bone lead studies are not directly comparable and do not represent the full spectrum of environmental lead exposure in teenagers. Noticeably, few teenage subjects with high lead exposure risks have been measured for bone lead. The two in vitro studies[29,30] analyzed cadaveric limbs using atomic absorption spectroscopy. Atomic absorption spectroscopy is regarded as the standard for lead analysis; however, it is a destructive analysis that limits its use for measuring lead in the bone of living subjects. Additionally, the bone lead levels of child cadavers may not be representative of healthy living children. The current study was conducted in a suburban community, with only one subject reporting a family history of lead poisoning; suburban children are generally anticipated to have lower lead exposure than urban children.[31] The Bellinger et al[18] study, which measured the bone lead levels of 67 of the original Needleman[32] cohort, has the lowest reported average bone lead value of all the reported studies, even though this population is predominantly urban children. However, the Bellinger et al study also has the highest variance and the greatest average measurement uncertainty of all the studies presented. Although these combined studies may not capture the full range of lead exposure for young adults, they do provide insight into the range of expected bone lead levels of teenagers living in the United States.

Although this study did not demonstrate an association with demographic or environmental factors and bone lead levels in teenagers, this does not indicate that demographic and environmental factors do not contribute to long-term storage of lead in bones. This study is limited by the low lead levels in this population and the reliance on surrogates to evaluate environmental lead exposure. Most of the studies to date have involved the measurement of bone lead levels among occupationally exposed groups and of older subjects.[8–10,12–14] In the Normative Aging Study, a large population-based cohort of older men (average age, 66.6 years), Hu et al[13] reported tibial bone lead levels ranging from <1 to 96 μg/g (mean, 21.6 μg/g; SD, 12.1 μg/g). These levels are much higher than those observed in the current study, because the men in this population have more years of environmental and occupational exposure contributing to body lead burden. In a study of women 20 to 36 years of age, Hu et al[14] reported bone lead levels ranging from -3 to 13 μg/g (mean, 4.5 μg/g; SD, 4.0 μg/g); these levels are similar to the values observed in the current investigation. In a cross-sectional study of female and male subjects 11 to 70 years of age, Kosnett et al[10] reported bone lead levels of -12 to 69 μg/g; bone lead levels for the 14 subjects <20 years of age were not statistically different from zero.

Power calculations indicate that this study had sufficient power to detect a difference of 1.9 to 2.5 μg/g bone lead for potential bone lead predictors (eg, sex, race, and decade of home construction); however, we were unable to detect such a difference. Currently, there are no comprehensive data on the biological relevance of bone lead concentrations in teens to determine whether a difference of 1 to 2 μg/g is of biological importance. Needleman et al[33] recently reported a provocative study suggesting that 11-year-olds with higher bone lead levels were more likely to be identified as antisocial and delinquent than those with lower bone lead levels. Al-

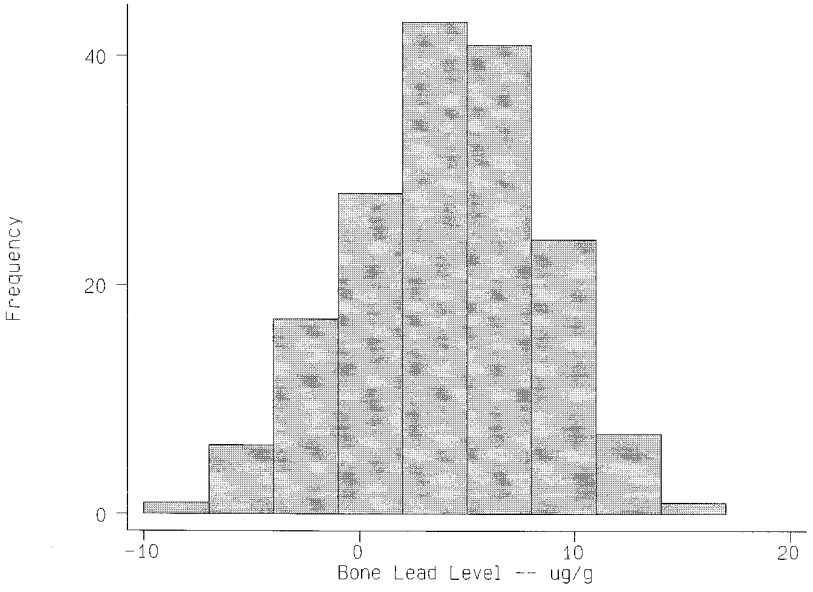

Fig 2. Distribution of bone lead concentrations in 168 suburban Boston teenagers.

TABLE 2. Summary of Bone Lead Studies of Teenagers and Young Adults

Study	Sample Size	Age Range (in Years)	Average Bone Lead Concentration (μg/g)	SD
In vitro studies				
Barry, 1981[5]	5	11–16	4.8*	1.9
Wittmers et al, 1988[30]	13	13–20	2.3	3.6
In vivo studies				
Bellinger et al, 1994[18]	67	18–22	1.6	4.9
Hoppin et al, 1995[11]	23	18–21	3.0	2.3
Current study	168	13–19	4.0	4.4

* Corrected for wet weight.

though bone lead was measured using a K-XRF device similar to the one in the current study, the analytical technique used to calculate bone lead concentration was different.[34] The method used by the Needleman group for estimating bone lead concentrations used only the Kβ peaks, which account for $<$20% of the lead emission spectrum.[22,34] Use of this method may result in values that are not directly comparable with the values reported here and elsewhere.

This current study suggests that bone lead levels in this suburban population are sufficiently low and uniform that no particular demographic or environmental factor influences bone lead concentrations. Alternatively, because turnover of bone is rapid during adolescence, the impact of environmental and demographic factors may be noticeable only after maximum height and bone mass and the accumulation of more lead are reached. Given the relatively slow integration rates of bone lead reported, ranging from 0.4 to 1.5 μg Pb/g bone/year observed in cross-sectional studies,[8,10,11,27,28] the differences in bone lead may be detectable only among subjects older than this age group.

Because of the lack of reported childhood lead exposure, these data are insufficient to test the hypothesis of whether early childhood lead exposure contributes to adult bone lead levels, as suggested by clinical observations,[35] or whether the dynamics of bone turnover in adolescence result in a dilution of early childhood lead exposures, as suggested by toxicokinetic modelers[7,36] in models based on animal data for bone-seeking elements such as lead. Longitudinal studies of populations with well-documented childhood lead exposure will be the only way to address this question adequately.

Environmental lead exposure was measured by surrogate measures, such as housing age and street traffic level. Although these measures were demonstrated to be predictive of in-home lead levels in this community,[19] they are not measures of actual exposure levels. Environmental data were not available for a majority of the study participants and, therefore, were not used in bone lead analysis. Additionally, other sources of lead besides home-based sources may be contributing to lead exposure in these teenagers; thus, relying solely on home exposures may underestimate the subjects' actual lead exposure.

In this study, the population variance was influenced significantly by measurement error. Future studies should use a variety of strategies to reduce the influence of measurement error. One strategy would be to conduct a study in a more highly exposed population and to focus the recruitment strategy on characteristics that reduce the measurement uncertainty. Among these teenage subjects, participants who were older, taller, and heavier had the lowest reported measurement uncertainty. To reduce measurement error, study protocols may be altered

either to increase the sampling time or to increase the number of measurements made on an individual. In previous work, we showed that by doubling the sampling time, the measurement uncertainty reduces by the $\sqrt{2}$, as expected by counting theory.[11] However, it is unlikely that a subject would be willing to be sampled for a period of >60 minutes. Because lead integrates into bone over the course of years, it would be feasible to collect multiple measurements on the same individual over a short period of time and use the average to obtain a more stable estimate of the individual actual bone lead measurement.

Bone lead measurement in teenagers represents an innovative approach to evaluate the long-term impact of environmental lead exposure. Although we were unable to demonstrate specific environmental contributions to bone lead levels in these suburban teens, we were able to indicate that exposure to lead is still occurring in this population. Future work among slightly older and more highly exposed populations may be warranted to ascertain the contribution of environmental lead exposures to bone lead levels in young populations.

ACKNOWLEDGMENTS

This work was supported by National Institute of Environmental Health Sciences Superfund P42-ES05947 and National Institute of Environmental Health Sciences National Research Service Award 5 T32 ES07069.

We thank John Dugan and Keri Dailey for their hard work at subject recruitment and measurement; and the students, staff, and administration of Randolph Junior/Senior High School for their assistance with this study.

REFERENCES

1. National Academy of Sciences, National Research Council. *Measuring Lead Exposure in Infants, Children, and Other Sensitive Populations.* Washington, DC: National Academy Press; 1993
2. Graziano JH. Validity of lead exposure markers in diagnosis and surveillance. *Clin Chem.* 1994;40:1387–1390
3. Rabinowitz MB, Wetherill GW, Kopple JD. Kinetic analysis of lead metabolism in healthy humans. *J Clin Invest.* 1976;58:260–270
4. Schroeder H, Tipton I. The human body burden of lead. *Arch Environ Health.* 1968;17:965–978
5. Barry PSI, Mossman D. Lead concentration in human tissues. *Br J Ind Med.* 1970;27:339–351
6. Rabinowitz MB. Toxicokinetics of bone lead. *Environ Health Perspect.* 1991;91:33–37
7. O'Flaherty EJ. Physiologically based models for bone seeking elements. IV. Kinetics of lead deposition in humans. *Toxicol Appl Pharmacol.* 1993; 118:16–29
8. Somervaille LJ, Chettle DR, Scott MC, Tennant DR, McKiernan MJ, Skilbeck A, Trethowan WN. In vivo tibia lead measurements as an index of cumulative exposure in occupationally exposed subjects. *Br J Ind Med.* 1988;45:174–181
9. Erkkila J, Armstrong R, Riihimaki V, et al. In vivo measurements of lead in bone at four anatomical sites: long term occupational and consequent endogenous exposure. *Br J Ind Med.* 1992;49:631–644
10. Kosnett MJ, Becker CE, Osterloh JD, Kelly TJ, Pasta DJ. Factors influencing bone lead concentration in a suburban community assessed by noninvasive k x-ray fluorescence. *JAMA.* 1994;271:197–203
11. Hoppin JH, Aro ACA, Williams PL, Hu H, Ryan PB. Validation of K-XRF bone lead measurement in young adults. *Environ Health Perspect.* 1995;103:78–83
12. Hu H, Aro ACA, Rotnitsky A. Bone lead measured by x-ray fluorescence: epidemiologic methods. *Environ Health Perspect.* 1995; 103(suppl 1):105–110
13. Hu H, Aro A, Payton M, et al. The relationship of bone and blood lead to hypertension: the Normative Aging Study. *JAMA.* 1996;275: 1171–1176
14. Hu H, Hashimoto D, Besser M. Levels of lead in blood and bone of women giving birth in a Boston hospital. *Arch Environ Health.* 1996;51: 52–58
15. Rosen JF, Markowitz ME, Bijur PE, Jenks ST, Wielopolski L, Kalef-Ezra JA, Slatkin DN. Sequential measurements of bone lead content by L x-ray fluorescence in $CaNa_2$ EDTA-treated lead-toxic children. *Environ Health Perspect.* 1991;93:271–277
16. Hu H, Milder FL, Burger DE. X-ray fluorescence: issues surrounding the application of a new tool for measuring bone lead burden. *Environ Res.* 1989;49:295–317
17. Preiss IL, Tariq MA. On the use of L X-ray fluorescence for bone lead evaluation. *J Radioanal Nucl Chem.* 1992;164:381–387
18. Bellinger D, Hu H, Titlebaum L, Needleman H. Attentional correlates of dentin and bone lead levels in adolescents. *Arch Environ Health.* 1994; 49:98–105
19. Hoppin JA, Elreedy S, Ryan PB. Validation of a self-administered lead exposure questionnaire among suburban teenagers. *Environ Res.* 1997. In press
20. Aro ACA, Todd AC, Amarasiriwardena C, Hu H. Improvements in the calibration of ^{109}Cd K x-ray fluorescence systems for measuring bone lead in vivo. *Phys Med Biol.* 1994;39:2263–2271
21. Todd AC, McNeill FE, Palethorpe JE, et al. In vivo x-ray fluorescence of lead in bone using K x-ray excitation with ^{109}Cd sources: radiation dosimetry studies. *Environ Res.* 1992;57:117–132
22. Chettle DR, Scott MC, Somervaille LJ. Lead in bone: sampling and quantitation using K x-rays excited by ^{109}Cd. *Environ Health Perspect.* 1991;91:49–55
23. Marquardt DW. An algorithm for least squares estimation of nonlinear parameters. *J Soc Indust Appl Math.* 1963;11:431–441
24. Stata Corporation. *Stata Reference Manual. Release 3.1.* 6th ed. College Station, TX: Stata Corporation, 1993
25. Hu H, Milder FL, Burger DE. The use of K x-ray fluorescence for measuring lead burden in epidemiological studies: high and low lead burdens and measurement uncertainty. *Environ Health Perspect.* 1991;94: 107–110
26. Somervaille LJ, Chettle DR, Scott MC, et al. Comparison of two in vitro methods of bone lead analysis and the implications for in vivo measurements. *Phys Med Biol.* 1986;31:1267–1274
27. Hu H, Milder FL, Burger DE. X-ray fluorescence measurements of lead burden in subjects with low-level community lead exposure. *Arch Environ Health.* 1990;45:335–341
28. Watanabe H, Hu H, Rotnitsky A. Correlates of bone and blood lead levels in carpenters. *Am J Ind Med.* 1994;26:255–264
29. Barry PSI. Concentrations of lead in the tissues of children. *Br J Ind Med.* 1981;38:61–71
30. Wittmers LE, Wallgren J, Alich A, Aufderheide AC, Rapp G. Lead in bone. IV. Distribution of lead in the human skeleton. *Arch Environ Health.* 1988;43:381–391
31. Brody DJ, Pirkle JL, Kramer RA, et al. Blood lead levels in the US population: phase 1 of the Third National Health and Nutrition Examination Survey (NHANES III, 1988 to 1991). *JAMA.* 1994;272: 277–285
32. Needleman HL, Gunnoe C, Leviton A, et al. Deficits in psychologic and classroom performance of children with elevated dentine lead levels. *N Engl J Med.* 1979;300:689–695
33. Needleman HL, Reiss JA, Tobin MJ, Biesecker GE, Greenhouse JB. Bone lead levels and delinquent behavior. *JAMA.* 1996;275:363–369
34. Hoppin JA, Ryan PB, Hu H, Aro ACA. Bone lead levels and delinquent behavior. *JAMA* 1996;275(letter, comment):1727
35. Goldman RH, White R, Kales SN, Hu H. Lead poisoning from mobilization of bone stores during thyrotoxicosis. *Am J Ind Med.* 1994;25: 417–424
36. Leggett RW. An age-specific kinetic model of lead metabolism in humans. *Environ Health Perspect.* 1993;101:598–616